

### In the Claims

1. (Currently Amended) A method for identifying a motif or a combination of motifs having a Boolean state of predetermined mutations in a set of sequences comprising:

a) aligning a set of sequences of ordered motifs represented by a single-character code on a programmed computer using a multiple sequence alignment program,

b) comparing a reference sequence with the set of sequences aligned in step (a),

c) identifying motifs not having mutated simultaneously or motifs having mutated simultaneously at least once on at least one sequence of the set and not having mutated on another sequence of said set, and

d) outputting the identified motifs to ~~at least one of a~~ computer controlled display, a memory, another computer, a network or a user, or physically transforming the identified motifs ; wherein the steps of the method are performed on a programmed computer.

2. (Original) The method according to claim 1, wherein the motif or the combination of motifs is a nucleotide or a combination of nucleotides and a subset of sequences is selected from sequences in a databank of nucleic acids.

3. (Currently Amended) The method according to claim 1, wherein the motif or the combination of motifs is an amino acid or a combination of amino acids and a subset of sequences is selected from sequences in a databank of polypeptides ~~and/or~~ or proteins.

4. (Currently Amended) The method according to claim 1, wherein the reference sequence is a wild-type sequence.

5. (Original) The method according to claim 1, wherein the reference sequence is a sequence comprising in a position i a motif present in position i in a predetermined number of sequences of step (a).

6. (Currently Amended) The method according to claim 1, wherein step (b) comprises:

forming a first numerical matrix A of dimensions NxM in which N designates a number of sequences and M designates a number of motifs of one sequence of said alignment, with value  $A_{i,j}$  being equal to a first value A1 when the motif of position i of sequence j with a value ranging from 0 to N is mutated in relation to a motif of position i of the reference sequence and equal to a second value A2 in the other cases,

forming two analysis matrices B and C of mutations in which this matrix is:

– a matrix B of unmutated couples, of couples which do not mutate simultaneously, of dimension MxM, value  $B_{i,k} = B_{k,i}$  being equal:

- to a first value B1 when  $A_{i,j} = A_{k,j} = A1$  irrespective of the value of j ranging from 0 to N,
- to a second value B2 in other cases;

– a matrix C of mutated couples of dimension MxM, value  $C_{k,i} = C_{i,k}$  being equal:

- to a second value C1 when  $A_{i,j} = A_{k,j}$  irrespective of the value of j ranging from 0 to N,
- to a first value C2 in the other cases;

determining for a set E of positions a coefficient  $R_E$  whose value is  $R_1$  when values  $B_{i,k}$  are equal to a second value B2, irrespective of the values of i and k belonging to set E of said positions,

determining for a set F of positions, a coefficient  $R_F$ , the value of which is  $R_1$  when values  $C_{i,k}$  are equal to second value C2, irrespective of the values of i and k belonging to set F of said positions;

wherein in the matrices, i and k designate positions and j designates a sequence.

7. (Currently Amended) The method according to claim 6, wherein positions of at least one of the sets E and/or F are designated by the user.

8. (Original) The method according to claim 6, wherein step (b) comprises a test step including generating a totality of combinations of possible positions, determining for each of said combinations the value of coefficients  $R_R$  or  $R_F$ , and retaining the combination corresponding to a largest set of positions coefficient  $R_E$  or  $R_F$  of which corresponds to said second value.

9. (Original) The method according to claim 1, wherein the set of sequences comprises sequences of motifs of pathogenic organisms having a high level of mutability.

10. (Original) The method according to claim 1, wherein the set of sequences comprises sequences of motifs of genes implicated in human, animal or plant pathologies having a high level of mutability.

11. (Withdrawn) An influenza vaccine comprising the motif or combination of motifs according to claim 1.

12. (Withdrawn) An HIV vaccine comprising the motif or combination of motifs according to claim 1.

13. (Withdrawn) A hepatitis C vaccine comprising the motif or combination of motifs according to claim 1.

14. (Withdrawn) A pharmaceutical composition for treatment of influenza comprising a therapeutically effective amount of the motif or combination of motifs according to claim 1.

15. (Withdrawn) A pharmaceutical composition for treatment of HIV comprising a therapeutically effective amount of the motif or combination of motifs according to claim 1.

16. (Withdrawn) A pharmaceutical composition for treatment of hepatitis C comprising a therapeutically effective amount of the motif or combination of motifs according to claim 1.

17. (Withdrawn) A method of treating influenza comprising administering a therapeutically effective amount of the pharmaceutical composition according to claim 14 to a patient in need thereof.

18. (Withdrawn) A method of treating HIV comprising administering a therapeutically effective amount of the pharmaceutical composition according to claim 15 to a patient in need thereof.

19. (Withdrawn) A method of treating hepatitis C comprising administering a therapeutically effective amount of the pharmaceutical composition according to claim 16 to a patient in need thereof.

20. (Original) The method according to claim 1, wherein the set of sequences of step (a) comprises all polypeptide sequences of different variants of a protease of human immunodeficiency virus.

21. (Withdrawn) The method according to claim 1, wherein the set of sequences of step (a) comprises all polypeptide sequences of different variants of a reverse transcriptase of human immunodeficiency virus.

22. (Withdrawn) The method according to claim 1, wherein the set of sequences of step (a) comprises all polypeptide sequences of different variants of integrase of human immunodeficiency virus.

23. (Withdrawn) The method according to claim 1, wherein the set of sequences of step (a) comprises all sequences of motifs of different variants of a gene or protein of neuraminidase of flu virus.

24. (Withdrawn) The method according to claim 1, wherein the set of sequences of step (a) comprises all sequences of motifs of different variants of a gene or protein of hemagglutinin of flu virus.

25. (Withdrawn) The method according to claim 1, wherein the set of sequences of step (a) comprises all sequences of motifs of different variants of a gene and/or protein of hepatitis C virus.

26. (Withdrawn) The method according to claim 1, wherein the set of sequences of step (a) comprises all sequences of motifs of different variants of a gene or protein HspA of bacterium *Helicobacter pylori*.

27. (Withdrawn) The method according to claim 1, wherein the subset of sequences of motifs selected in step (a) comprises all sequences of different variants of a gene or protein of type HA adhesin of bacterium *Escherichia coli*.

28. (Currently Amended) The method according to claim 1, further comprising, after step (c), a step ~~(d)~~ (e) of comparing motifs identified in step (c) with known drug resistances to observed mutations.

29. (Currently Amended) The method according to claim 1, further comprising, after step (c), a step ~~(e)~~ (f) of comparing motifs identified in step (c) with motifs of sequences implicated in at least one of a catalytic site and/or in sites and a site linked by noncompetitive inhibitors.

30. (Withdrawn) A method of preparing an oligonucleotide sequence comprising: identifying a nucleotide sequence according to claim 1, and synthesizing said sequence.

31. (Withdrawn) A method of preparing a polypeptide sequence comprising: identifying an amino acid sequence according to claim 1, and synthesizing said sequence.

32. (New) A method for identifying a motif or a combination of motifs having a Boolean state of predetermined mutations in a set of sequences comprising:

a) aligning a set of sequences of ordered motifs represented by a single-character code on a programmed computer using a CLUSTAL algorithm based multiple sequence alignment program or a Hidden Markov Model algorithm based multiple sequence alignment program,

b) comparing a reference sequence with the set of sequences aligned in step (a),

c) identifying motifs not having mutated simultaneously or motifs having mutated simultaneously at least once on at least one sequence of the set and not having mutated on another sequence of said set, and

d) outputting the identified motifs to a computer controlled display; wherein the steps of the method are performed on a programmed computer.

33. (New) The method of Claim 32 wherein the CLUSTAL algorithm is the CLUSTAL W algorithm.